REMARKS

Claims 29-43 have been canceled without prejudice or disclaimer. Claims 44-75 have been added and therefore are pending in the present application. Claims 44-75 are supported throughout the specification, including the original claims. For example, the % identities of the amino acid sequences of the parents and variants recited in claims 44 and 46-51 are supported at page 16, lines 12-19 of the specification.

The specification has been amended to add a Cross-Reference to Related Applications section and to delete embedded hyperlinks.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Restriction Requirement

The Office maintained and supplemented the restriction requirement. Currently, restriction is required between the following groups:

Group I – claims drawn to galactanase variants,

Group II – claims drawn to nucleic acid sequences encoding a galactanase variant,

Group III – claims drawn to animal feed compositions, and

Group IV – claims drawn to methods for hydrolyzing lactose.

The Office contends that the claims lack unity of invention because UnitProt Accession No. Q9Y7F8 discloses a variant A90S. This is respectfully traversed.

As discussed below, UniProt Accession No. Q9Y7F8 discloses a wild-type *Aspergillus tubingensis* arabinogalactan endo-1,4-beta-galactosidase. Thus, UniProt Accession No. Q9Y7F8 does not disclose or suggest a variant of a parent Glycoside Hydrolase Family 53 galactanase, comprising one or more alterations, as claimed herein.

Applicants therefore respectfully submit that the restriction requirement is improper and request withdrawal thereof.

Moreover, even if restriction was proper, Applicants submit that new claim 44 links Groups I, II and IV. Therefore, upon allowance of the linking claim, the restriction requirement as to the linked inventions should be withdrawn and all claims within the linked inventions should be examined in the instant application.

II. The Objection to the Specification

The Office objected to the specification because it contains embedded hyperlinks. The hyperlinks have been deleted, as requested by the Examiner. Applicants therefore submit that this objection has been overcome.

III. The Objection to the Specification

The Office objected to the specification because Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 121 [sic, 119(e)].

The specification has been amended to add a reference to the prior applications, as requested by the Examiner. Applicants therefore submit that this objection has been overcome.

IV. The Objection to Claims 29, 31-32, 34, 36 and 38

The Office objected to claims 29, 31-32, 34, 36 and 38 as encompassing non-elected subject matter. This is respectfully traversed.

As discussed above, the restriction requirement is improper and should be withdrawn. Moreover, there would be no burden on the Office to examine positions 90, 91, 181, 303, 305, and 313.

The Office also objected to claim 38 because the recitations "K-6P", "S-4P", and L-2P" should be "K6P", "S4P", and L2P, respectively. This objection is respectfully traversed.

The recitations in claim 38 are correct. As described in the specification, each position is the number of the corresponding amino acid residue in SEQ ID NO: 1. Thus, when aligned with SEQ ID NO: 1, the positions recited in the claims correspond to -6, -4, and -2. Applicants therefore submit that this objection has been overcome.

V. The Rejection of Claims 29-41 under 35 U.S.C. 112

Claims 29-41 are rejected under 35 U.S.C. 112 as failing to comply with the written description requirement. This rejection is respectfully traversed.

It is well settled that "[t]he test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter ..." *In re Kaslow*, 217 USPQ 1089, 1096 (Fed. Cir. 1983). The written description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971).

As set forth in Federal Circuit decisions, a specification complies with the written description requirement if it provides "a precise definition, such as by structure, formula, chemical name, or physical properties of the claimed subject matter sufficient to distinguish it from other materials." *See, e.g., University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398, 1404 (Fed. Cir. 1997); *Enzo Biochem v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002).

Moreover, the Written Description Training Materials published by the USPTO on March 25, 2008 provides guidance in applying the written description requirement. Particularly relevant to the instant application is Example 11, "Percent Identity" and more specifically, Example 11B "Art-Recognized Structure-Function Correlation Present." Example 11B provides "Claim 2" which is a claim to an isolated nucleic acid sequence that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2; wherein the polypeptide has activity Y. The specification of Example 11B discloses the reduction to practice of only a single species that encodes SEQ ID NO: 2 and has activity Y, *i.e.*, nucleic acid SEQ ID NO: 1, but the specification does not teach which 15% of the amino acids will vary from SEQ ID NO: 2, nor any other polypeptides with 85% identity to SEQ ID NO: 2 that have activity Y. However, the knowledge in the art of the genetic code would allow one skilled in the art, with the aid of a computer, to list all of the nucleotide sequences capable of encoding a polypeptide with at least 85% identity to SEQ ID NO: 2, thus identifying all polypeptides having at least 85% identity to SEQ ID NO: 2. Further, Example 11B provides that the specification identifies two domains responsible for the activity Y, *i.e.*, a binding domain and a catalytic domain, and predicts that conservative mutations in these domains will result in the protein having activity Y, and those of ordinary skill in the art would expect that many of the conservative substitutions would result in a protein having the required activity. Additionally, substitutions outside of the functional domains were predicted to have little effect on activity Y. Thus, a correlation exists between the function of the claimed protein and the structure of the disclosed binding and catalytic domains. The conclusion is that the written description requirement is satisfied for Claim 2 of Example 11B.

Applicants respectfully submit that the claims of the instant application comply with the written description requirement under 35 U.S.C. 112, first paragraph.

The claimed invention is directed to variants of a parent Glycoside Hydrolase Family 53 galactanase, comprising an alteration in at least one of the following positions: 90, 91, 181, 303, 305, and 313, wherein (a) the parent Glycoside Hydrolase Family 53 galactanase comprises an amino acid sequence which is at least 80% identical to SEQ ID NO: 1; and (b) the variant comprises an amino acid sequence which is at least 80% identical to SEQ ID NO: 1.

For the reasons discussed in Example 11B of the recently-published Written Description Training Materials, one skilled in the art can list all of the amino acid sequences of parents and variants with 80% identity to SEQ ID NO: 1.

Furthermore, the class of galactanases is well characterized and those skilled in the art can recognize the conserved regions among galactanases. Moreover, Applicants disclose several parent galactanases and disclose numerous variants of the present invention. Moreover, just as one skilled in the art can recognize mutations to the catalytic and binding domains and substitutions outside of the catalytic and binding domains of SEQ ID NO: 2 in Example 11B which would result in a polypeptide having activity Y, persons skilled in the art also can recognize mutations to the catalytic domain and substitutions outside of the catalytic domain in the polypeptide of SEQ ID NO: 1 or another parent of the instant invention, which would result in a polypeptide having galactanase activity.

Applicants respectfully submit that the claims of the instant application meet the requirement for written description under 35 U.S.C. 112, first paragraph, by disclosing relevant, identifying characteristics, *e.g.*, the structure of SEQ ID NO: 1, and by functional characteristics, *i.e.*, galactanase activity, coupled with the known correlation between function and structure.

Moreover, given the high degree of identity recited in the claims, a high degree of predictability exists as to the structure and function of polypeptide falling within the claims.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. The Rejection of Claims 29-41 under 35 U.S.C. 112

Claims 29-41 are rejected under 35 U.S.C. 112 as failing to comply with the enablement requirement. This rejection is respectfully traversed.

It is well settled that an assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974). See also *U.S. v. Telectronics*, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974); *Ex parte Hitzeman*, 9 U.S.P.Q.2d 1821 (BPAI 1988).

Moreover, in the absence of any evidence or apparent reason why compounds do not possess the disclosed utility, the allegation of utility in the specification must be accepted as correct. *In re Kamal*, 158 U.S.P.Q. 320 (C.C.P.A. 1968). See also *In re Stark*, 172 U.S.P.Q.

402, 406 n. 4 (C.C.P.A. 1972) (the burden is upon the Patent Office to set forth reasonable grounds in support of its contention that a claim reads on inoperable subject matter).

It is well settled that "[t]he first paragraph of section 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance." *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). Moreover, "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of section 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 169 U.S.P.Q. at 369.

"The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art ... The test is not quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed ..." *Ex parte Jackson*, 217 U.S.P.Q. 804 (Bd. Pat. App. 1982).

Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

The reasoning provided in the Office Action is that the specification does not provide enablement for any variant polypeptide of any structure of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration at position 90 having galactanase activity or any variant polypeptide, which is 25% sequence identity to SEQ ID NO: 1. This is respectfully traversed.

The present invention relates to variants of a parent glycoside hydrolase Family 53 galactanase, comprising an alteration in at least one of the following positions: 90, 91, 181, 303, 305, and 313, wherein (a) the parent Glycoside Hydrolase Family 53 galactanase

comprises an amino acid sequence which is at least 80% identical to SEQ ID NO: 1; and (b) the variant comprises an amino acid sequence which is at least 80% identical to SEQ ID NO: 1.

The specification discloses numerous wild-type parent galactanases. Specifically, in the table at pages 13-15, the specification discloses 18 different bacterial and fungal parent galactanases. It would be clear to persons skilled in the art that the amino acids at any of positions 90, 91, 181, 303, 305, and 313 (using SEQ ID NO: 1 as numbering) could be modified in accordance with the present invention. Moreover, the specification discloses other sources of parent galactanases. *See, e.g.*, column 15, line 13 – column 16, line 5 of the specification.

Furthermore, the specification contains an extensive disclosure of the positions which can be modified as well as the specific mutations which can be introduced into a parent galactanase. It is well within the skill of the art to produce the claimed galactanase variants using Applicants' disclosure.

Finally, the specification discloses several assays for determining galactanase activity. *See, e.g.*, Examples 3-6.

We draw the Examiner's attention to *In re Angstadt*, 190 U.S.P.Q. 214 (C.C.P.A. 1976). In *Angstadt*, the claimed process of preparing hydroperoxides used a metal salt complex as a catalyst. The specification disclosed catalysts that worked and some that gave little or no yield of hydroperoxides. The claims were rejected for lack of enablement, specifically as requiring undue experimentation to find useful catalysts. This rejection was reversed by the CCPA.

In holding that the claims did satisfy 35 USC 112, the Court observed, 190 U.S.P.Q. at 218:

> We cannot agree with the board that appellants' disclosure is not sufficient to enable one of ordinary skill in the art to practice the invention without undue experimentation. We note that many chemical processes, and catalytic processes particularly, are unpredictable, [citation omitted] and that the scope of enablement varies inversely with the degree of unpredictability involved, [citation omitted]. That this particular process is unpredictable is demonstrated further by appellants in their specification. Appellants have disclosed forty examples; one of these examples yields no hydroperoxides in the final product. Also, appellants have expressly indicated in their specification that some of these organometallic complex catalysts 'yield *** no hydroperoxides in the final product.'
>
> Appellants have apparently not disclosed every catalyst which will work; they have apparently not disclosed every catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with every species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with 'thousands' of catalysts along with information as to whether each exhibits catalytic behavior

> resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid 'literal' infringement of such claims by merely finding another analogous catalyst complex which could be used in 'forming hydroperoxides.'

This admonition applies with equal force to the present application, which exemplifies numerous parent and variant galactanases. To require more would fly in the face of the *Angstadt* holding.

The Court, 190 USPQ at 218, recognized that some experimentation might be necessary for the skilled worker to select non-exemplified catalysts for use:

> Appellants have, in effect, provided those skilled in this art with a large but finite list of transition metal salts from which to choose in preparing such a complex catalyst. Appellants have actually carried out 40 runs using various transition metal salts and hexaalkylphosphoramides. If one skilled in this art wished to make and use a transition metal salt other than those disclosed in appellants' 40 runs, he would merely read appellants' specification for directions how to make and use the catalyst complex to oxidize the alkylaromatic hydrocarbons, and could then determine whether hydroperoxides are, in fact, formed. The process discovered by appellants is not complicated, and there is no indication that special equipment or unusual reaction conditions must be provided when practicing the invention. One skilled in this art would merely have to substitute the correct mass of a transition metal salt for the transition metal salts disclosed in appellants' 40 runs. Thus, we have no basis for concluding that persons skilled in this art, armed with the specification and its 40 working examples, would not easily be able to determine which catalyst complexes within the scope of the claims work to produce hydroperoxides and which do not.

However, while <u>some</u> experimentation might be necessary, as long as the experimentation was not "undue experimentation," the claims would not violate 35 USC 112, *Angstadt*, <u>Id</u>:

> Since appellants have supplied the list of catalysts and have taught how to make and how to use them, we believe that the experimentation required to determine which catalysts will produce hydroperoxides <u>would not be undue and certainly would not 'require ingenuity beyond that to be expected of one of ordinary skill in the art.'</u> (Emphasis added).

As in *Angstadt*, the present application identifies numerous parent and variant galactanases. While some experimentation might be necessary to identify other non-exemplified variant galactanases, such experimentation would require carrying out a simple process without special equipment or unusual reaction conditions, as in *Angstadt.* This experimentation, if required, "would not be undue and certainly would not 'require ingenuity beyond that expected of one of ordinary skill in the art.'" (*Angstadt*, 190 U.S.P.Q. at 218). Certainly, there is no evidence of record to the contrary.

The Office alleges that "The art clearly teaches that modification of a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are tolerant of modification and which ones are conserved is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity." This is respectfully traversed.

As of Applicants' filing date, persons of ordinary skill in the art were able to routinely identify essential amino acids in the amino acid sequence of a polypeptide. Indeed, one skilled in the art could predict which modifications, if any, would result in a loss of the desired activity/utility. Moreover, the Office selectively chooses a few references (Branden et al., Witkowski et al. and Seffernick et al.) and ignores the many references which disclose active variants.

Applicants refer the Examiner to the precedential opinion from the BPAI, *Ex parte Kubin*, 83 U.S.P.Q.2d 1410 (Bd. Pat. App. & Int. 2007). In *Kubin*, the claimed invention was isolated polynucleotides (1) that encode polypeptides which are at least 80% identical to amino acids 22-221 of SEQ ID NO: 2 (the extracellular domain of NAIL without the signal sequence) and (2) that bind to CD48. The specification provided two working examples; a DNA encoding NAIL, i.e. SEQ ID NO: 1, and NAIL's coding sequence with up and downstream noncoding sequences, i.e. SEQ ID NO: 3, each of which encode the polypeptide of SEQ ID NO: 2. The specification did not disclose any variants of SEQ ID NO: 2, but the specification taught how to make the variants, calculate percent identity between the disclosed sequence and the variants, and how to test the variant sequence to determine if it binds to CD48. In the Board's finding of facts, the Board determined the level of skill in the art of molecular biology was high, that methods of making the claimed sequences and screening for activity were known in the art and described in the specification, that the experimentation involved to produce other sequences within the scope of the claims was well within the skill of those in the art, the experimentation would have been routine, and undue experimentation to practice the invention would not be

required. *Kubin* at 1415. Although the Board stated that molecular biology is generally an unpredictable art, the Board appropriately considered the remaining *Wands* factors, particularly "the state of the art" and the "relative skill of those in the art," *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988), and found that the amount of experimentation to practice the full scope of the claimed invention could be extensive, but routine. Thus, the Board concluded the specification was enabling for the full scope of the claimed invention. *Kubin* at 1416.

Similarly, in the present case, the level of skill in the relevant art (molecular biology) is high and the techniques required to identify, make and use the variants commensurate in scope with the claimed invention are well known to those skilled in the art. As discussed above, one skilled in the art can recognize which parent and variant polypeptides have an amino acid sequence with at least 80% identity with the sequence of SEQ ID NO: 1, and can recognize what substitutions within or outside of the conserved functional domains can be reasonably tolerated without affecting the galactanase activity. Additionally, the specification discloses a number of routine techniques that can be used to determine galactanase activity.

For the foregoing reasons, Applicants submit that the specification as filed contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation, and meets the enablement requirement under 35 U.S.C. 112, first paragraph. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

VII. The Rejection of Claims 29-35 and 38-41 under 35 U.S.C. 102

Claims 29-35 and 38-41 are rejected under 35 U.S.C. 102(b) as being anticipate by UnitProt Acession No. Q9Y7F8. This rejection is respectfully traversed.

UniProt Accession No. Q9Y7F8 discloses a wild-type *Aspergillus tubingensis* arabinogalactan endo-1,4-beta-galactosidase. Thus, UniProt Accession No. Q9Y7F8 does not disclose or suggest a variant of a parent Glycoside Hydrolase Family 53 galactanase, comprising one or more alterations, as claimed herein.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

VIII. The Rejection of Claims 36 and 37 under 35 U.S.C. 102

Claims 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Kofod et al. (U.S. Patent No. 6,329,185). This rejection is respectfully traversed.

Kofod et al. disclose a wild-type galactanase obtained from *Meripilus giganteus* and galactanases having an amino acid sequence with at least 70% identity to the amino acid sequence of the *Meripilus giganteus* galactanase.

However, Kofod et al. do not disclose or suggest a variant of a parent Glycoside Hydrolase Family 53 galactanase, comprising one or more alterations at positions 90, 91, 181, 303, 305, and/or 313 wherein each alteration is an insertion, substitution or deletion, as claimed herein.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

IX. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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